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Docket No.: GMI-059
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Janine Schuurman, *et al.*

Application No.: 10/714353

Confirmation No.: 6363

Filed: November 14, 2003

Art Unit: 1643

For: HUMAN MONOCLONAL ANTIBODIES
AGAINST CD25

Examiner: Bristol, Lynn Anne

DECLARATION BY DR. Jan GJ van de Winkel UNDER 37 C.F.R. §1.132

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Dr. Jan GJ van de Winkel, declare the following:

1. I, Dr. Jan GJ van de Winkel, am presently the Chief Scientific Officer at Genmab A/S, the assignee of the above-referenced patent application. I am also Professor of Immunology at Utrecht University. My *curriculum vitae* is attached herewith as Appendix 1.
2. I have reviewed claims 22-24, 28-30, 32-34, and 36-38 of the above-referenced application, drawn to an isolated human monoclonal anti-human CD25 antibody comprising at least a particular heavy and light chain variable region CDR3 sequence (e.g., SEQ ID NOs:25 and 28), including conservative sequence modifications thereof.
3. I understand that claims 22-24, 28-30, 32-34, and 36-38 of the above-referenced application have been rejected as not being enabled. Specifically, the Examiner asserts that the claimed antibodies, defined by at least particular heavy and light chain CDR3 sequences, are not enabled. The Examiner also asserts that the claimed antibodies are not enabled with respect to "conservative sequence modifications" within the recited CDR regions.
4. It is my opinion that, prior to the filing date of the present application, it was well within the skill of the art to predictably design and generate human anti-CD25 antibodies that share the same binding specificity, based on common CDR3 heavy and light chain variable region sequences (e.g., human CD25-binding antibodies having a heavy chain CDR3 sequence as defined in the claims, but having differing CDR2 and CDR1 sequences). It is also my opinion that it was well within the skill of the art to have identified residues within the claimed variable and CDR regions that were amenable to conservative sequence substitutions (*i.e.*, residues that could be conservatively substituted without removing antibody binding). Indeed, the production of antibodies based on common CDR3 sequences, as well as the identification of residues within the CDR domains of such antibodies that are

amenable to conservative modifications, would have required only routine procedures, and particularly in view of the short length of these sequences, would not have involved undue experimentation. Indeed, the various methods and materials that were available, well before the filing date of the present application, are evidenced by the pre-filing references submitted with the Amendment and Response being filed along with this Declaration (discussed below).

5. In particular, the references summarized in Appendix A include a number of studies which have identified the heavy chain CDR3 region as being determinative of antigen-binding specificity. Moreover, it was found that the heavy chain CDR3 sequence alone can retain and confer antigen specificity when placed into a different antibody framework (*i.e.*, along with different CDR2 and CDR1 sequences). This is evidenced, for example, by Klimka *et al.* (2000) British J. of Cancer 83(2):252-260; Beiboer *et al.* (2000) J. Mol. Biol. 296:833-849; Rader *et al.* (1998) PNAS USA 95:8910-8915; Barbas *et al.* (1994) 116 J. Am. Chem. Soc. 2161-2162; Barbas *et al.* (1995) 92 PNAS USA 2529-2533; and Ditzel *et al.* (1996) 157 J. of Immunol. 739-749 (Appendices B-G, respectively), as well as the other references summarized in Appendix A.

6. With respect to the Examiner's position that the presently claimed antibodies which include conservative sequence modifications within the CDRs are not enabled, I refer to the references summarized in Appendix I (and described in detail in the accompanying Amendment and Response, *e.g.*, Brummell *et al.*, (1993) Biochem. 32:1180-1187; Kobayashi *et al.*, (1999) Protein Eng. 12(10):879-884; and Burks *et al.* (1997) PNAS USA 94:412-417; attached as Appendices J, K, and L, respectively). These references demonstrate the high level of skill in the art that existed prior to the filing date of the present application, and the fact that it did not require undue burden to have identified residues within the CDR domains of an antibody which could be conservatively modified without removing antigen binding.

7. In conclusion, it is my opinion, as supported by the foregoing representative pre-filing publications, that the knowledge and skill in the art at the time the present application was filed, combined with the teachings contained in the present specification, would have enabled one skilled in the art to have made and used the currently claimed antibodies, defined at least by the claimed heavy and light chain CDR3 sequences, as well as conservative sequence modifications thereof, without undue experimentation.

8. I have been warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 or the United States Code, and that such willful and false statements may jeopardize the validity of the subject application or any patent resulting therefrom, and declare that all statements made of our own knowledge are true and that all statements made on information and belief are believed to be true.

By: 

Date: 2-2-2007



Update: April 6, 2006

CURRICULUM VITAE

PERSONAL DATA

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Date of birth : March 1, 1961
Place of birth : Venray, The Netherlands
Citizenship : Dutch
Marital status : Married, four children

EDUCATION AND PROFESSIONAL BACKGROUND

- 1973-1979 : Secondary school (Gymnasium- β) "Het Jerusalem", Venray, The Netherlands.
- 1979 - 1985 : Biology study, University of Nijmegen, The Netherlands
* Master of Science (M.Sc.) in Biology: april 1985 (*cum laude*)
- Principal subject: Physiology, Department of Physiology
- Subsidiary subjects: Immunology, Department of Nephrology and Biochemistry, Department of Biochemistry
- 1985 - 1988 : Graduate work, Department of Nephrology, University-Hospital Nijmegen. Research fellow of the Netherlands Organization for Scientific Research (NWO).
* Doctoral degree (Ph.D.): October 7, 1988.
- Thesis: *Human monocyte Fc γ receptors*.
- 1988 - 1989 : Post-doctoral Fellow, Department of Experimental Immunology, Utrecht University, The Netherlands.
- Jan - Dec 1990 : Visiting Scientist, Department of Internal Medicine, Ohio State University, Columbus (OH), USA.
- 1990 - 1992 : Assistant Professor, Department of Experimental Immunology, Utrecht University, The Netherlands.
- 1992 - 1996 : Associate Professor, Department of Immunology, Utrecht University, The Netherlands.
- 1996 - present : Professor, Department of Immunology, Utrecht University, The Netherlands.
- 1996 - 2000 : Scientific Director, Medarex Europe, Utrecht, The Netherlands.
- 1998 - 2000 : Vice President, Medarex Europe, Utrecht, The Netherlands.
- 1999 - 2001 : Chief Scientific Officer, Genmab A/S, Copenhagen, Denmark.
- 2001 - 2003 : Senior Vice President & Chief Scientific Officer, Genmab A/S, Copenhagen, Denmark.
- 2003 - present : Executive Vice President & Chief Scientific Officer, Genmab A/S, Copenhagen, Denmark.

HONORS / AWARDS

- 1990 Recipient of a NATO Science-exchange Fellowship from the Netherlands Organization for Scientific Research.
- 1996 Recipient of the *Dolph O. Adams* Award from The Society for Leukocyte Biology for the *most cited paper over the past five years* for a 1991 review "Biology of human Immunoglobulin G Fc receptors" (ref. 26).
- 2000 Winner *Nalinaj Fernando Memorial Award* for the best research article into primary immunodeficiency. "The role of Fc gamma receptor polymorphisms and C3 in the immune defense against *Neisseria meningitidis* in complement-deficient individuals". December 2000, British Society for Immunology (ref. 154).
- 2000 *Van Loghem Laureate 2000*, Dutch Society for Immunology.

PROFESSIONAL SOCIETIES AND ACTIVITIES

- Member American Association of Immunologists, Dutch Society for Immunology.
- Member, Editorial board, Immunogenetics (1997 - 2002).
- Regular reviewer for Molecular and Cellular Biology, Immunology Today, Journal of Immunology, Blood, Immunology, Journal of Leukocyte Biology, Arthritis & Rheumatism, Journal of Immunological Methods, European Journal of Immunology, EMBO Journal, Leukemia, Molecular Immunology, Immunogenetics, Clinical & Experimental Immunology, Kidney International, Journal of Clinical Investigation, Nature.
- Regular grant reviewer for ~~The Wellcome Trust, The National Science Foundation~~ (USA), The Netherlands Organization for Scientific Research, The Arthritis & Rheumatism Council (U.K.), Nationaal Reumafonds, NWO-Technology Foundation STW.
- Secretary, Study section Inflammation (901-12), Netherlands Organization for Scientific Research (1993 - 1996).
- Chairman, Study section Inflammation (901-12), Netherlands Organization for Scientific Research (1996 - 1999).
- Treasurer, Educational Committee, Dutch Society for Immunology (1995 - 1998).
- Member, Educational Committee, Dutch Society for Immunology (1998 - 2002).
- Member, Scientific Advisory Board, IDM, Paris, France (1994 - 1997).
- Consultant, Medarex Inc., Princeton (New Jersey), USA (1993 - present).
- Member, Board of advisors, The Thai Network for Biomedical Research (1997).
- Organizer, Vth World Conference on Bispecific Antibodies, Volendam (June 25-28, 1997), The Netherlands.
- Organizer, Annual Scientific Masterclasses, Utrecht Institute for Infection & Immunity (1993 - 1998).
- Chairman, Award committee, "The Centeon Award for Innovative Breakthroughs in Immunology" (1997 - 2001).
- Member, Scientific Council, Netherlands Cancer Foundation (NKB/KWF; 1998 - 2001).
- Member, Board of Division "Genetics, Microbiology & Immunology", Netherlands Organization for Scientific Research (1998 - 2000).
- Member, Organizing Committee, VIth International Conference on Bispecific Antibodies, Pacific Grove, California, USA (July 28 - August 1, 1999).
- Member, Supervisory Board of Directors, Central animal laboratory, Utrecht University (1999 - 2001).
- Member, Scientific Advisory Board, Biotech Turnaround Fund (BTF), Haarlem, The Netherlands (2000-present)
- Member, Organizing Committee, VIIth International Antibody Conference on Targeted Cellular Cytotoxicity, Hartley Wintney, UK (July 2001).
- Member, Curatorium, chair in Ophthalmology focussing on internal eye infection, Utrecht University (2003 - present).
- Organizer, Workshop "Immune-intervention for cancer and inflammation", 38th Annual Scientific Meeting of the European Society for Clinical Investigation, Utrecht, The Netherlands (April 2004).
- Member, Scientific Advisory Board, Thuja Capital Healthcare Fund, Utrecht, The Netherlands (2006 - present).

GRADUATE STUDENTS

Supervised 30 graduate students

PUBLISHED PAPERS

Published more than 250 scientific papers. The following papers were published since 2003 :

1. Van de Winkel, J.G.J., and C.L. Anderson. CD32: Cluster report:
In **Leucocyte Typing V** (S. Schlossman et al., Ed.), Oxford University Press, Oxford, 1995; 823-826.
2. Van den Herik-Oudijk, I.E., N.A.C. Westerdaal, M. de Haas, L. Kemper, P.J.A. Capel, A.E.G.Kr. von dem Borne, and J.G.J. van de Winkel. Binding Heterogeneity within the CD32 panel of monoclonal antibodies. In **Leucocyte Typing V** (S. Schlossman et al., Ed.), Oxford University Press, Oxford, 1995; 832-835.
3. Sanders, L.A.M., R.G. Feldman, M.M. Voorhorst-Ogink, M. de Haas, G.T. Rijkers, P.J.A. Capel, B.J.M. Zegers, and J.G.J. van de Winkel. Human IgG Fc receptor IIA (CD32) polymorphism and IgG2-mediated bacterial phagocytosis by neutrophils. **Infect. Immunity** 1995; 63: 73-81.

4. Haagen, I.-A., A.J.G. Geerars, M.R. Clark, and J.G.J. van de Winkel. Interaction of human monocyte Fc γ receptors with rat IgG2b: a new indicator for the Fc γ RIIa (R-H131) polymorphism. **J. Immunol.** 1995; 154: 1852-1860.
5. Van den Herik-Oudijk, I.E., P.J.A. Capel, T. van der Bruggen, and J.G.J. van de Winkel. Identification of signalling motifs within human Fc γ RIIa and Fc γ RIIb isoforms. **Blood** 1995; 85: 2202-2211.
6. Van de Winkel, J.G.J., A.P.M. de Wit, L.K. Ernst, P.J.A. Capel, and J.L. Ceuppens. Molecular basis for a familial defect in phagocyte expression of Fc γ receptor I (CD64). **J. Immunol.** 1995; 154: 2896-2903.
7. Cambier, J., M. Daeron, W. Fridman, J. Gergely, J.-P. Kinet, R. Klausner, R. Lynch, B. Malissen, I. Pecht, E. Reinherz, J. Ravetch, M. Reth, L. Samelson, M. Sandor, A. Schreiber, B. Seed, C. Terhorst, J. van de Winkel, and A. Weiss. New nomenclature for the Reth motif (or ARH1/TAM/ARAM/YXXL). **Immunol. Today** 1995; 16: 110.
8. Pfefferkorn, L.C., J.G.J. van de Winkel, and S.L. Swink. A novel role for IgG-Fc; transductional potentiation for human high affinity Fc γ receptor (Fc γ RI) signalling. **J. Biol. Chem.** 1995; 270: 8164-8171.
9. Kwack, K. J.S. Verbeek, J.G.J. van de Winkel, P.J.A. Capel, M. Nambu, M. Hagen, J.V. Weinstock, R.G. Lynch, and M. Sandor. Functional consequences of the interaction between T cell antigen receptors and Fc γ Rs on T cells. **Immunol. Lett.** 1995; 44: 139-143.
10. De Wit, A.P.M., H.C. Morton, P.J.A. Capel, and J.G.J. van de Winkel. Structure of the gene for the human myeloid IgA Fc receptor (CD89). **J. Immunol.** 1995; 155: 1203-1209.
11. Bredius, R.G.M., B.H.F. Derkx, C.A.P. Fijen, R.S. Weening, J.G.J. van de Winkel, and T.A. Out. Fc γ RIIa (CD32) allotype R131 as a risk factor for fulminant meningococcal septic shock. In **Progress in Immune Deficiency V** (I. Caragol, T. Espanol, G. Fontan, and N. Matamoros, Eds.) Springer-Verlag Iberica, 1995: 191-194.
12. Sanders, E.A.M., B.J.M. Zegers, J.G.J. van de Winkel, G.T. Rijkers, and M.M. Voorhorst-Ogink. Fc γ receptor Ila (CD32) heterogeneity in patients with recurrent bacterial respiratory tract infections. In **Progress in Immune Deficiency V** (I. Caragol, T. Espanol, G. Fontan, and N. Matamoros, Eds.) Springer-Verlag Iberica, 1995: 195-196.

13. Heijnen, I.A.F.M., and J.G.J. van de Winkel. A human Fc γ RI/CD64 transgenic model for *in vivo* analysis of (bispecific) antibody therapeutics. **J. Hematother.** 1995; 4: 351-356.
14. Repp, R., T. Valerius, G. Wieland, W. Becker, H. Steininger, Y. Deo, M. Gramatzki, J.G.J. van de Winkel, N. Lang, and J.R. Kalden. Stimulated PMN in immunotherapy of breast cancer with a bispecific antibody to Fc γ RI and Her-2/ Neu (MDX210). **J. Hematother.** 1995; 4: 415-421.
15. Vossen, A.C.T.M., G.J.M. Tibbe, M.J. Kröös, J.G.J. van de Winkel, R. Benner, and H.F.J. Savelkoul. Fc-receptor binding of anti-CD3 monoclonal antibodies is not essential for immunosuppression, but triggers cytokine-related side effects. **Eur. J. Immunol.** 1995; 25: 1492-1496.
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17. Van den Herik-Oudijk, I.E., M.W.H. Ter Bekke, M.J. Tempelman, P.J.A. Capel, and J.G.J. van de Winkel. Functional differences between two Fc receptor ITAM signalling motifs. **Blood** 1995; 86: 3302-3307.
18. Morton, H.C., I.E. van den Herik-Oudijk, P. Vossebeld, A. Snijders, A.J. Verhoeven, P.J.A. Capel, and J.G.J. van de Winkel. Functional association between the human myeloid IgA Fc receptor (CD89) and FcR γ chain: molecular basis for CD89/FcR γ chain association. **J. Biol. Chem.** 1995; 270: 29781-29787.
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20. Heijnen, I.A.F.M., M.J. van Vugt, N.A. Fanger, R.F. Graziano, A.P.M. de Wit, F.M.A. Hofhuis, P.M. Guyre, P.J.A. Capel, J.S. Verbeek, and J.G.J. van de Winkel. Antigen targeting to myeloid-specific human Fc γ RI/CD64 triggers enhanced antibody responses in transgenic mice. **J. Clin. Invest.** 1996; 97: 331-338
21. Van de Winkel, J.G.J., and P.J.A. Capel [Editors]. **Human IgG Fc Receptors**, R.G. Landes Company, Austin, TX, USA, 1996.

22. Van den Herik-Oudijk, I.E., J.S. Verbeek, P.J.A. Capel, and J.G.J. van de Winkel. Fc γ R on mononuclear cells. In **Human IgG Fc receptors** (J.G.J. van de Winkel and P.J.A. Capel, Eds.). R.G. Landes Company, Austin, TX, USA, pp. 57-78, 1996.
23. Morton, H.C., A.E. Schiel, S.W.J. Janssen, and J.G.J. van de Winkel. Alternatively spliced forms of the human myeloid Fc α receptor (CD89) in neutrophils. **Immunogenetics** 1996; 43: 246-247.
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25. Van Vugt, M.J., I.A.F.M. Heijnen, P.J.A. Capel, S.Y. Park, C. Ra, T. Saito, J.S. Verbeek, and J.G.J. van de Winkel. Fc γ R chain is essential for both surface expression and function of human Fc γ RI (CD64) *in vivo*. **Blood** 1996; 87: 3593-3599.
26. Kumpel, B.M., J.G.J. van de Winkel, N.A.C. Westerdal, A.G. Hadley, J.-M. Dugoujon, and A. Blancher. Antigen topography is critical for interaction of IgG2 anti-red cell antibodies with Fc γ receptors. **Brit. J. Haematol.** 1996; 94: 175-183.
27. Groenink, J. J. Spijker, I.E. van den Herik-Oudijk, L. Boeije, G. Rook, L. Aarden, R. Smeenk, J.G.J. van de Winkel, and M.F. van den Broek. On the interaction between agalactosyl-IgG and Fc γ receptors. **Eur. J. Immunol.** 1996; 26: 1404-1407.
28. Kruger, M., J.G.J. van de Winkel, A.P.M. de Wit, L. Coorevits, M. Casteels-Van Daele, and J.L. Ceuppens. Granulocyte-Macrophage Colony-Stimulating Factor rapidly downregulates CD14 expression on monocytes. **Immunology** 1996; 89: 89-95.
28. Morton, H.C., M. van Egmond, and J.G.J. van de Winkel. Structure and function of human IgA Fc receptors (Fc α R). **Crit. Rev. Immunol.** 1996; 16: 423-440.
29. Hazenbos, W.L.W., J.E. Gessner, F.M.A. Hofhuis, H. Kuipers, D. Meyer, I.A.F.M. Heijnen, R.E. Schmidt, M. Sandor, P.J.A. Capel, M. Daeron, J.G.J. van de Winkel, and J.S. Verbeek. Impaired IgG-dependent Anaphylaxis and Arthus reaction in Fc γ RIII (CD16) deficient mice. **Immunity** 1996; 5: 181-188.

30. Llewellyn-Jones, C., P. Cole, D. Kumararatne, and J.G.J. van de Winkel. The role of cellular immune responses in chronic pulmonary disease. In **Issues in Infection; The interaction between lung defences and bacteria - time for a reappraisal** (R.A. Stockley and S.L. Hill, Eds.), Cambridge Medical Publications, Worthing, West Sussex, U.K., pp. 13-15, 1996.
31. Van Vugt, M.J., I.E. van den Herik-Oudijk, and J.G.J. van de Winkel. Binding of PE-Cy5 conjugates to the human high affinity receptor for IgG (CD64). **Blood** 1996; 88: 2358-2360.
32. Worth, R.G., L. Mayo-Bond, J.G.J. van de Winkel, R.F. Todd III, and H.R. Petty. CR3 (α M β 2; CD11b/CD18) restores IgG-dependent phagocytosis in transfectants expressing a phagocytosis-defective Fc γ RIIA (CD32) tail-minus mutant. **J. Immunol.** 1996; 157: 5660-5665.
33. Van Dongen, J.J.M., C.G. Figdor, J.G.J. van de Winkel, and J. Borst. Receptoren in **Medische Immunologie** (R. Benner, J.J.M. van Dongen, W. van Ewijk, and J.J. Haaijman, Eds.), Wetenschappelijke uitgeverij Bunge, Utrecht, 1996, pp. 126-170.
34. Nibbering, P.H., E. Broug-Holub, A.C. Bezemer, R. Jansen, J.G.J. van de Winkel, and M.F. Geertsma. Phagocytosis and intracellular killing of serum-opsonized staphylococcus aureus by mouse fibroblasts expressing human Fc γ receptor type IIa (CD32). **Front. in Biosci.** 1996; 1: a24-32.
35. Rascu, A., R. Repp, N.A.C. Westerdal, J.R. Kalden, and J.G.J. van de Winkel. Clinical relevance of Fc γ receptor polymorphisms. **Ann. N.Y. Acad. Sci.** 1997; 815: 282-295.
36. Deo, Y.M., R.F. Graziano, R. Repp, and J.G.J. van de Winkel. Clinical significance of IgG Fc receptors and Fc γ R-directed immunotherapies. **Immunol. Today** 1997; 18: 127-135.
37. Stockmeyer, B., T. Valerius, R. Repp, I.A.F.M. Heijnen, H.J. Bühring, Y.M. Deo, J.R. Kalden, M. Gramatzki, and J.G.J. van de Winkel. Preclinical studies with Fc γ R bispecific antibodies and Granulocyte Colony-stimulating Factor-primed neutrophils as effector cells against HER-2/neu overexpressing breast cancer. **Cancer Res.** 1997; 57: 696-701.
38. Valerius, T., D. Elsässer, R. Repp, J.G.J. van de Winkel, M. Gramatzki, and M. Glennie. HLA class II antibodies recruit activated neutrophils for treatment of B cell malignancies. **Leukemia and Lymphoma** 1997; 26: 261-269.

39. Poole, A., J.M. Gibbins, M. Turner, M.J. van Vugt, J.G.J. van de Winkel, T. Saito, V.L.J. Tybulewicz, and S.P. Watson. The Fc receptor γ -chain and the tyrosine kinase Syk are essential for activation of mouse platelets by collagen. **EMBO J.** 1997; 16: 2333-2341.
40. Heijnen, I.A.F.M., and J.G.J. van de Winkel. Human IgG Fc receptors. **Int. Rev. Immunol.** 1997; 16: 29-55.
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42. Valerius, T., B. Stockmeyer, A.B. van Spriel, R.F. Graziano, I.E. van den Herik-Oudijk, R. Repp, Y. Deo, J. Lund, J.R. Kalden, M. Gramatzki, and J.G.J. van de Winkel. Fc α RI (CD89) as a novel trigger molecule for bispecific antibody therapy. **Blood** 1997; 90: 4485-4492.
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44. Van de Winkel, J.G.J., B. Bast, and G.C. de Gast. Immunotherapeutic potential of bispecific antibodies. **Immunol. Today** 1997; 18: 562-564.
45. Gratama, J.W., R. van der Linden, B. van der Holt, R.L.H. Bolhuis, and J.G.J. van de Winkel. Analysis of factors contributing to the formation of mononuclear cell aggregates ('escapees') in flow cytometric immunophenotyping. **Cytometry** 1997; 29: 250-260.
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GRANTS

1990	NATO Science-exchange Fellowship via the Netherlands Organization for Scientific Research (NWO)
1993-1994	European Community (Human Capital and Mobility) grant "Molecular characterization of the human IgA Fc receptor"
1993-1997	Medarex Research grant "Role of the human high affinity IgG Fc receptor I (CD64) in antigen presentation"
1994-1996	Wellcome Trust Research Grant "Biological characterization of the human IgA Fc receptor"
1994-1998	Netherlands Organization for Scientific Research (NWO) grant (901-12-174) "Biological implications of human IgG Fc receptor I (CD64) complexity"
1995-1997	Medarex Research grant "Evaluation of CD64-bispecifics for anti-fungal therapy"
1995-1999	Netherlands Organization for Scientific Research (NWO) grant (901-12-214) "Molecular and Functional characterization of human IgA Fc receptors"
1995-1999	Netherlands Organization for Scientific Research (NWO) grant (950-10-624) "Relevance of IgG Fc receptor polymorphism of PMNs for the epidemiology of meningococcal disease"
1996-1997	Utrecht University (Hoofdlijn Infectie en Immuniteit) grant "Immuuntherapie van schimmelinfecties met G-CSF en CD64-bispecifieke antistoffen"
1997	NWO-Japanese Society for the Promotion of Science (JSPS) grant (JB 97-48) "Fc receptor polymorphisms and periodontal disease susceptibility"
1997-1999	EC Training grant (BIO4-97-5084) "Functional dissection of the role of human antibody subclasses in immunity to encapsulated bacterial infections"
1997-2001	Dutch Cancer Foundation (KWF/NKB) grant (UU 97-1517) "G-CSF-mobilized neutrophils as effector cells for immunotherapy in breast carcinoma"
1997-2001	Dutch Kidney Foundation grant (C96.1610) "Fc-receptor polymorfismen bij ge-systematiseerde lupus erythematosus: betekenis voor de klinische expressie van de ziekte"
1997-2001	EC Biotechnology grant (BIO-CT97-2216) "Cellular Vaccines"
1998-2000	Genvlag grant UMC "Immuno-allotypering van Fc receptor polymorfismen bij autoimmuunziekten, infectieziekten en polyneuropathieën"
1998-2000	BTS grant (BTS98110) "Mobilization and modulation of the natural immune system for immunotherapy"
1998-2002	WKZ Sterproject "Mucosale immuniteit en infecties; IgA, Fc receptoren en vaccinatie"
2000-2003	NWO-Technology Foundation STW grant (UFA.5157) "Selective elimination of inflammatory macrophages through immunotoxins: a novel concept in the treatment of rheumatoid arthritis"
2000-2004	National Rheumatism Foundation grant (NR 99-1-402) "Modulation of arthritis and cartilage damage via Fc receptors"
2001-2004	National Rheumatism Foundation grant (00-2-302) "(Pre-)klinisch onderzoek naar het effect van immunotoxinen in de selectieve eliminatie van macrofagen"

- bij reumatoïde arthritis"
- 2001-2005 Dutch Cancer Foundation (KWF/NKB) grant (UU 2001-2496) "Development of concepts for induction of potent anti-tumor vaccine responses"
- 2001-2005 Dutch Cancer Foundation (KWF/NKB) grant (UU 2001-2431) "Human immunoglobulin A receptor (FcαRI, CD89) as target for immunotherapy"
- 2002-2006 Dutch Cancer Foundation (KWF/NKB) grant (UU 2002-2706) "Mechanisms of cooperation of FcαRI (CD89) and Mac-1 (CD11b/CD18) in tumor cytotoxicity; implications for immunotherapy"
- 2002-2005 NWO-DFG grant "Chimeric human IgA antibodies for tumor therapy"

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